INVESTIGATION OF LACTAMS

XXII.* PROTONATION AND HYDROLYSIS OF α-ENAMINES OF CAPRO- AND VALEROLACTAMS

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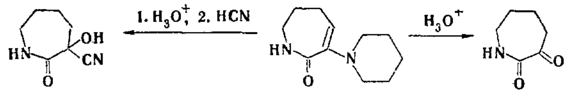
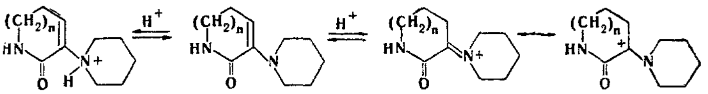
From an examination of the PMR spectra, polarographic data, and molecular models of α-enamines of capro- and valerolactams, it is concluded that there is a different degree of conjugation of the p electrons of the piperidine nitrogen with the enamine double bond and that this explains the differences in the tendency of these compounds to undergo hydrolysis.

A convenient method for the synthesis of α-enamines of valero- (I) and caprolactams (II) by reaction of the α,α-dichlorolactams with piperidine was previously developed in [2]. Despite the complete, as it were, structural similarity of enamines I and II, they differ considerably with respect to their chemical behavior. Thus, enamine II is readily hydrolyzed in acidic media at 0°C to α-oxocaprolactam III [1], but the α-enamine of 2-piperidone (I) cannot be hydrolyzed under these conditions or under more severe conditions. The reaction of II with NaCN similarly leads to a high yield of α-hydroxy-α-cyanocaprolactam (IV) [1], while enamine I cannot be converted to the corresponding cyanohydrin.



IV II III

The behavior of II in acidic media is typical for enamines, the hydrolysis of which to ketones proceeds to give products in high yields [3]; however, the anomalous stability of enamine I under the same conditions has made it necessary to make a more detailed study of its properties. The measurement of the basicities of I and II in nitromethane gave unexpected results: the ΔpK_a values of these enamines were 3.93 and 1.6, respectively, i.e., the basicity of seven-membered enamine II is higher by more than two orders of magnitude than that of the six-membered I. It is apparent that the reason for this considerable change in the basicity in a series of structurally similar compounds can only be a change in the site of protonation. It is logical to assume that C-protonation (high basicity) occurs preferably in the case of enamine II, while protonation of I takes place at the nitrogen atom:



V I, II IIa IIb

I, V n = 1; II, IIa, IIb n = 2

Because of the resonance IIa ⟷ IIb, the C-protonated form is considerably more inclined to undergo nucleophilic attack (and, consequently, to undergo hydrolysis) than the N-protonated form (V).

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*See [1] for communication XXI.

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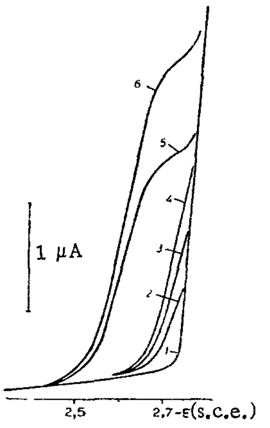

Fig. 1

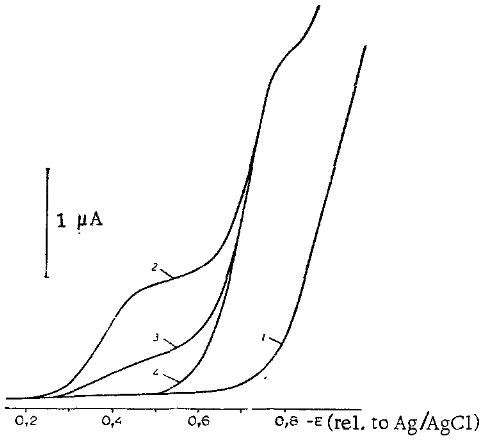

Fig. 2

Fig. 1. Polarograms of I and II with a saturated $(CH_3)_4NI$ base electrolyte in DMF: 1) base electrolyte curve; 2) $c_{II} = 0.46$ mmole; 3) $c_{II} = 0.88$ mmole; 4) $c_{II} = 1.25$ mmole; 5) $c_I = 1.08$ mmole; 6) $c_I = 1.55$ mmole. S.c.e is saturated calomel electrode.

Fig. 2. Polarograms of II with a base electrolyte consisting of 0.17 N CF_3COOH in MDF saturated with KCl: 1) Base electrolyte curve; 2) $c_{II} = 1.56$ mmole (the curve was recorded immediately after introduction of the substance into solution); 3) the same after 2 min; 4) the same after 5 min.

The signal of the vinyl proton in the PMR spectrum of enamine II (5.06 ppm) is substantially shifted to the strong-field side as compared with enamine I (5.54 ppm); this is due to the higher electron density on $C_{(4)}$ in II. It has been shown [4] that enamines in anhydrous dimethylformamide (DMF) are reduced with substantially greater difficulty than ethylene compounds and that the center of attack of the electron is the β-carbon atom. Correspondingly, both enamines I and II are reduced in one step, apparently with the consumption of two electrons [4], and enamine II is reduced at more negative potentials than I. The reduction wave of enamine II is masked to a considerable degree by the discharge current of the base electrolyte, and, in this connection, the precise measurement of the half-wave potential is difficult. To a first approximation, the diffusion coefficients of I and II were assumed to be equal, and the potential of that point of the curve at which the current is equal to half the limiting (calculated) current was taken for $E_{1/2}$ of enamine II (the diffusion coefficient of enamine I was determined from the Il'kovich equation and was $5.42 \cdot 10^{-6}$ cm· sec^{-2}). The half-wave potentials of I and II are, respectively, −2.58 and −2.73 V relative to a saturated calomel electrode (see Fig. 1). This sort of substantial difficulty in the reduction of enamine II as compared with enamine I is in agreement with the PMR spectral data and also indicates the relatively high electron density on the double bond of the former. A primary consequence of this is the difference in the site of protonation of these compounds. An examination of the PMR spectrum of I in CF_3COOH shows that in this case N-protonation occurs: the signal of the vinyl proton is shifted to the weak-field region (7.33 ppm) because of the increase in the electron-acceptor strength of the substituent (the piperidinium cation) [5]. In addition to N-protonation, C-protonation occurs to a considerable degree for enamine II [5]. In the presence of strong proton donors (a 0.17 N solution of CF_3COOH) the reduction of enamine II in DMF is markedly facilitated. In this case, two waves are observed on the polarogram, and the first falls rapidly with time, while the overall current remains constant (Fig. 2). The second wave is identical to the reduction wave of lactam III (the addition of III to the solution of cation $II \cdot H^+$ leads to a proportional increase in the second wave). The decrease with time in the first wave with the simultaneous formation of α-oxocaprolactam III is in good agreement with the chemical data on the hydrolysis of enamine II in acidic media and provides unambiguous evidence that the first wave corresponds to reduction of the immonium cation (IIa ⟷ IIb). In fact, the reduction of this cation should proceed incomparably more readily [6] than reduction of the double bond of the enamine; this is observed experimentally. Thus, the difference in the properties of enamines I and II is explained by a change in the site of protonation; this is associated with the presence of higher electron density on the β-carbon atom of enamine II as compared with I. To explain the latter, the assumption of a greater degree of conjugation of the unshared pair of electrons of the nitrogen atom with the C=C bond in II has been advanced; this was completely confirmed in an examination of the molecular models of both enamines. The steric hindrance to conjugation in I, i.e., the overlapping of the van der Waals radii of the protons attached to $C_{(4)}$ of the piperidine ring and the $C_{(2)}$ atom of the piperidine ring leads to a considerable disruption of the p–π conjugation and, as a result of this, to a decrease in the electron density on the enamine C=C bond. In contrast to this, complete overlapping of the p electrons of the nitrogen atom and the π electrons of the double bond is possible in enamine II. Thus, the substantial differences in the properties of the α-enamines of lactams I and II are due to the different degree of conjugation of the pair of p electrons of the nitrogen atom with the C=C bond as a consequence of the different steric interaction of the hydrogen atoms attached to $C_{(4)}$ of the lactam ring and the α-protons of the piperidine ring.

EXPERIMENTAL

The study of the polarographic behavior and the measurement of the ΔpK_a (CH_3NO_2) values of enamines I and II were performed via previously described methods [4, 7]. The ΔpK_a value (CH_3NO_2) is the difference in the pK_a values of diphenylguanidine and the test substance in nitromethane. The PMR spectra were recorded with a JNM-4H-100 spectrometer with tetramethylsilane as the internal standard.

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